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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,477	01/09/2007	Masao Sudoh	Q94121	2361

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EXAMINER	
KATAKAM, SUDHAKAR	

ART UNIT	PAPER NUMBER
1621	

NOTIFICATION DATE	DELIVERY MODE
06/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,477	SUDOH ET AL.	
	Examiner	Art Unit	
	SUDHAKAR KATAKAM	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-16,18,19,23-31 and 33-36* is/are pending in the application.

4a) Of the above claim(s) *18,19 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-16,23-28 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/11/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the application

1. Receipt of Applicant's request for continued examination filed on 19 April 2010 is acknowledged.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 April 2010 has been entered.

2. Receipt of Applicant's remarks and arguments filed on 19 April 2010 is acknowledged. With regard to the 103(a) rejection, the applicants' arguments are not found persuasive. However, upon further consideration, in view of applicants' amendments to the claims, a new ground(s) of rejection is made in view of different interpretation of the previously applied reference, newly found prior art references, and provide an explanation of the rejection.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 7-16, 23-28, and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Hasegawa et al** (Bull.Chem.Soc.Jpn. 2000, 73, 423-428) or **JP 8291106** in view of **Ohuchida et al** (US 6,201,021), **Black** (US 6,043,223), **Toda et al** (US 6,608,221) and **Takada et al** (US 2002/0022738 A1).

Hasegawa et al disclose an optically active (R)-2-propyloctanoic acid, valuable therapeutic agent for neurodegenerative diseases such as Alzheimer's disease (see equation 1 in page 423 and introduction).

JP 8291106 also discloses a salt of optically active (2R)-2-propyloctanoic acid for use in treating neurodegenerative disorders (see Abstract, translation is pending, and attached Derwent abstract).

The difference between the instant claims and the references is that the references teach the compound or it's salt and silent on the source of metal ion, pH and the concentration of the components in the medicament.

However, the source of metal ions is very well established in the art. The most common sources of metal ions in the art are di or tri-sodium phosphate, sodium or potassium hydroxide etc. One skilled person in the art would be motivated to choose a

metal ion source as a matter of choice depending on variables such as compound solubility factors or availability or cost etc. Furthermore a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Applicants are invited to provide a showing which is commensurate in scope with the claimed invention that clearly demonstrate that the claimed metal ion source result in some unexpected property over the prior art.

There are many prior art available, which teaches the source of metal ions to stabilize the drug compounds. The following examples illustrate the multiple utilities of metal ion sources, such as sodium phosphate, for small peptides to drug compounds.

Black teaches use of phosphate buffer saline solution as a carrier for the bradykinin, comprises 10-40 micrograms/mL of bradykinin and 0.09% phosphate buffered saline solution [col. 5, lines 41-45]. **Black** also teaches infusion preparation of bradykinin that is dissolved in aqueous solution containing sodium hydroxide and phosphate buffered saline solution [col. 5, lines 47-62]. Preparation of infusions for drugs, such as (2R)-2-propyloctanoic acid, are known in the art. Also the process of adjusting pH using buffers is also very well known procedure in the art.

Toda et al teach that (2R)-2-propyloctanoic acid, which is produced after the reductive reaction, is extracted with sodium hydroxide, it is clear that the sodium salt found in (2R)-2-propyloctanoic acid is produced in this series [see example 1].

Ohuchida et al teach suitable basic metal ions for the preparation of salts of pentanoic acid derivatives [col.17, lines 1-24].

Takada et al teach a process to improve the solubility of the drug compound and thereby providing a solution thereof and some kinds of drug products using the solution, moreover providing a solution of higher concentration and a high-dosage drug product using the solution, and in order to improve the solubility of drug compounds, which can be accomplished by adding at least one pH adjuster selected from tri-sodium phosphate, a hydrate thereof, sodium hydroxide or potassium hydroxide to the solution [see 0008 - 0010].

With regard to new limitation, micelle water dispersion, the meaning of micelle water dispersion, according to applicants' specification in page 23, the aggregates formed by the compound with basic metal ion are homogeneously dispersed in the medium water and its properties are not significantly different from those of conventional aqueous solutions. The composition of cited prior art and their conditions are similar to applicants' composition, and therefore, it is expected to have micelle water dispersion of liquid of the compound.

With regard to claims 14 and 34, the plastic container as claimed by applicants is nothing but capsule. Please note that the capsule technology is well established in the art. Applicants are invited to provide a showing which is commensurate in scope with the claimed invention that clearly demonstrate that the claimed container result in some unexpected property over the prior art.

Therefore, it would have been obvious to a person of ordinary skill in the art at the time of the invention to use the teachings of the above cited references and known methods, to make the composition of (2R)-2-propyloctanoic acid with basic metal ions, from the art, and to make the instant applicants medicament with a reasonable expectation of success. One would have been motivated to arrive instant claims because **Hasegawa et al** teach "preparation of (2R)-2-propyloctanoic acid" and this compound is a therapeutic agent of neurodegenerative diseases such as Alzheimer's disease. **Takada et al** teach a process to improve the solubility of the drug compound using the sodium phosphate. Therefore, one would combine the teachings of the references in order to provide for a medicament mixing the (2R)-2-propyloctanoic acid with a basic metal ion to facilitate the better stability of the drug composition in storage. For the foregoing reasons the instant claims are made obvious.

Modifying such process is prima facie obvious because an ordinary artisan would be motivated to explore the known metal ions sources from the art to make the drug composition more stable or more economical advantages over the other, since it is within the scope to optimize the conditions through a routine experimentation.

6. Claims 1, 7-16, 23-28, and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Honjo et al** (EP 1 415 668 A1) in view of **Nakaoka et al** (JP 07285911 A) and **Takada et al** (US 2002/0022738 A1).

Honjo et al teach a pharmaceutical composition for treating or preventing cerebral ischemic disease preferably comprises an astroctic function improving agent, represented by the formula **(I)**. Among the astrocyte function-improving agents used in

the invention, preferred embodiments are (R)-2-propyloctanoic acid and a non-toxic salt or hydrate thereof [see 0011].

Honjo et al also teach a compound represented by the formula (I) may be converted into the corresponding salts by the common method. Non-toxic and water-soluble salts are preferable. Suitable salts include, for example, salts of alkali metals (sodium, potassium, etc.), salts of alkaline earth metals etc., among which sodium salt is particularly preferable [see 0017].

Honjo et al also teach a compound represented by the formula (I) may be converted into the corresponding acid addition salts by the common method. Non-toxic and water-soluble acid addition salts are preferable. Suitable acid addition salts include, for example, inorganic acid salts, such as phosphate or nitrate etc. [see 0018].

Honjo et al deficient in the sense that it fails to teach the amount of basic metal ion in the composition.

The amount of basic metal ion in the composition is considered as an optimizable parameter. It is important to control the pH of the composition by adjusting the concentration of buffer solution, in this case metal salt of phosphoric acid, which is well known phosphate buffer in the laboratories. Nevertheless, the following secondary prior art cure the deficiency of **Honjo et al**.

Nakaoka et al teach an aliphatic monocarboxylic acid composition, composed of one or more kinds of aliphatic monocarboxylic acids of formula R-COOH (R is a 5-21C straight or branched-chain alkyl or alkenyl) in combination with one or more kinds of

inorganic salts selected from metal phosphates, metal phosphinates and metal sulfites. The inorganic metal salt is preferably one or more compounds selected from alkali metal phosphates and alkaline earth metal phosphates. The amount of the inorganic metal salt is preferably 5-10,000ppm based on the aliphatic carboxylic acid. [see Abstract, full translation is pending].

Takada et al teach a process to improve the solubility of the drug compound and thereby providing a solution thereof and some kinds of drug products using the solution, moreover providing a solution of higher concentration and a high-dosage drug product using the solution, and in order to improve the solubility of drug compounds, which can be accomplished by adding at least one pH adjuster selected from tri-sodium phosphate, a hydrate thereof, sodium hydroxide or potassium hydroxide to the solution [see 0008 - 0010].

With regard to new limitation, micelle water dispersion, the meaning of micelle water dispersion, according to applicants' specification in page 23, the aggregates formed by the compound with basic metal ion are homogeneously dispersed in the medium water and its properties are not significantly different from those of conventional aqueous solutions. **Honjo et al** composition conditions are similar to applicants' composition, and therefore, it is expected to have micelle water dispersion of liquid of the compound.

With regard to claims 14 and 34, the plastic container as claimed by applicants is nothing but capsule. Please note that the capsule technology is well established in the art. Applicants are invited to provide a showing which is commensurate in scope with

the claimed invention that clearly demonstrate that the claimed container result in some unexpected property over the prior art.

Therefore, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to combine the teachings of the above cited references, to make the instant applicants medicament with a reasonable expectation of success. One would combine the teachings of the references in order to provide for a medicament mixing the (2R)-2-propyloctanoic acid with a basic metal ion to facilitate the better stability of the drug composition in storage.

Modifying such process is prima facie obvious because an ordinary artisan would be motivated to explore the known metal ions sources from the art to make the drug composition more stable or more economical advantages over the other, since it is within the scope to optimize the conditions through a routine experimentation.

Response to Arguments

7. Applicant's arguments filed on 19 April 2010 have been fully considered but they are not persuasive.

The examiner acknowledges applicants argument that the **Black** teaches the use of sodium hydroxide to dissolve zaprinst and there is no teaching or suggestion of mixing (2R)-2-propyloctanoic acid with sodium phosphate.

The examiner contends, however, that the purpose of **Black** is to show the use of metal ion sources, such as sodium phosphate, to stabilize the drug compounds or peptides. Therefore, it is appropriate in combination with the other references. The

amount of salt in the composition is depends on the compound and varied from compound to compound.

The examiner acknowledges applicants argument that **Takada et al** do not teach or suggest any similarity between the drug compound of **Takada et al** (2R)-2-propyloctanoic acid or salt thereof.

The examiner contends, however, that **Takada et al** teach a process to improve the solubility of the drug compound and thereby providing a solution thereof and some kinds of drug products using the solution, moreover providing a solution of higher concentration and a high-dosage drug product using the solution, and in order to improve the solubility of drug compounds, which can be accomplished by adding at least one pH adjuster selected from tri-sodium phosphate, a hydrate thereof, sodium hydroxide or potassium hydroxide to the solution. Therefore, the process of **Takada et al** can be applied to 2R)-2-propyloctanoic acid.

The examiner acknowledges applicants argument that the cited prior art teach the salt of 2R)-2-propyloctanoic acid, but the present invention does not relate to salt.

The examiner contends, however, that the claims require (2R)-2-propyloctanoic acid or a salt thereof and basic metal ion source. Even if it is acid form, which on combination with metal ion source, becomes salt.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sudhakar Katakam/
Examiner, Art Unit 1621